Image AF 1723

PATENT
Attorney Docket No. 440446/PALL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

BORMANN et al.

Application No. 09/806,322

Art Unit: 1723

Examiner: Krishman Menon

Filed: March 29, 2001

For: BIOLOGICAL FLUID FILTER AND SYSTEM

TRANSMITTAL OF APPELLANTS' APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.192, appellants hereby submit Appellants' Brief on Appeal in triplicate.

The items checked below are appropriate:

1. Status of Appellants

This application is on behalf of ☒ other than a small entity or ☐ a small entity.

2. Fee for Filing Brief on Appeal

Pursuant to 37 CFR 1.17(c), the fee for filing the Brief on Appeal is for: ☒ other than a small entity or ☐ a small entity.

Brief Fee Due $330.00

3. Oral Hearing

☐ Appellants request an oral hearing in accordance with 37 CFR 1.194.

4. Extension of Time

☐ Appellants petition for a one-month extension of time under 37 CFR 1.136, the fee for which is $110.00.

☒ Appellants believe that no extension of time is required. However, this conditional petition is being made to provide for the possibility that appellants have inadvertently overlooked the need for a petition and fee for extension of time.

Extension fee due with this request: $

5. Total Fee Due

The total fee due is:

Brief on Appeal Fee	$330.00
Request for Oral Hearing	$ 0.00
Extension Fee (if any)	$ 0.00

Total Fee Due: $330.00

6. Fee Payment

☐ Attached is a check in the sum of $.
☒ Charge Account No. 12-1216 the sum of $330.00. A duplicate of this transmittal is attached.

7. Fee Deficiency

☒ If any additional fee is required in connection with this communication, charge Account No. 12-1216. A duplicate copy of this transmittal is attached.

Respectfully submitted,

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Date: 5 Jan. 2004

Appeal Brief Transmittal (Revised 10/1/03)

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APPELLANTS' BRIEF ON APPEAL

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In support of this appeal, Appellants now submit their Brief on Appeal. A Notice of Appeal was filed on November 7, 2003.

Real party in interest

The real party in interest is the Assignee, Pall Corporation.

Related appeals and interferences

None.

Status of Claims

As filed (with a preliminary amendment upon entering the National phase under 35 USC 371), the application contained claims 1-14 and 17-20. During prosecution, claims 3 and 8 were additionally cancelled, and claims 21-25 were added, so that claims 1, 2, 4-7, 9-14 and 17-25 are pending in the application. Claims 1, 2, 4-7, 9-14 and 17-25 are finally rejected. The rejection of claims 1, 2, 4-7, 9-14 and 17-25 is appealed and those claims appear in the Appendix.

Status of Amendments

There were no amendments filed pursuant to 37 C.F.R. §1.116.

Summary of Invention

The present invention pertains to filter devices and methods for providing a plasma-containing biological fluid (e.g., for use as a transfusion product) that has been depleted of leukocytes and red blood cells.

In one embodiment, the filter device for processing a biological fluid comprises a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet; a filter disposed in the housing across the fluid flow path, the filter comprising: a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element; wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes and red blood cells therethrough.

In another embodiment, the filter device for processing a biological fluid comprises a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet; a filter disposed in the housing across the fluid flow path, the filter comprising: a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element; wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

The benefits of such filters and using such filters are several-fold. The presence of leukocytes in transfusion products is undesirable, as they can cause adverse effects (e.g., a febrile reaction) in the patient receiving the transfusion. Moreover, the presence of a significant level of red blood cells in the transfusion product can lead to an adverse immune response by the patient.

Issues

The issues on appeal are:

Whether the invention defined by appealed claims 1, 2, 4-7, 9-14 and 17-25 would have been obvious under 35 U.S.C. § 103 to one of ordinary skill in the art in view of U.S. Patent No. 5,587,070 to Pall *et al.* (hereinafter referred to as "Pall '070").

Grouping of Claims

For the purposes of this appeal, there are two groups of claims to be given separate consideration. These claims do not stand or fall together.

The first group of claims (Group I) consists of independent claims 1, 10, 12, 14, and 21, and dependent claims 4-7, 9, 13, 17, 18, and 22-24. The second group of claims (Group II) consists of independent claims 2, 11, and 20, and dependent claims 19 and 25.

Argument

The Group I Claims

The Group I claims, claims 1, 4-7, 9, 10, 12-14, 17, 18, and 21-24, were rejected under 35 U.S.C. § 103 as unpatentable over Pall '070.

While the June 10, 2003 Office Action acknowledges that Pall '070 does not disclose the invention as claimed in the Group I claims, the Office Action states that Pall '070 teaches a filter comprising a porous fibrous leukocyte depletion medium having a CWST of greater than 70 dynes/cm, and teaches a filter of 5 microns or less, and concludes it would have been obvious to one of ordinary skill in the art at the time of the invention to put a fibrous leukocyte depletion filter and a membrane in the same housing in series to obtain the desired separation of biological fluids while reducing the volume hold-up of the biological fluids. The Office Action also refers to compactness, ease of fabrication, and less conduit length.

The Office Action's position is incorrect.

While Pall '070 refers to a porous fibrous leukocyte depletion medium and a membrane (the Office Action has noted references to a membrane as a separation medium in

the non-centrifugal separation device), there is no suggestion of placing them in the same housing (*cf.*, Figure 1 in the instant application).

Rather, '070 Pall discloses the media in separate devices, e.g., at col. 18, lines 43-50: "In the embodiment of the invention which includes a separation assembly **14**, preferably a non-centrifugal separation device, the supernatant layer (e.g., PRP) may be passed through a leucocyte depletion assembly, and then passed through the non-centrifugal separation device **14**, where it may be processed and separated into components. . ." *See also*, Figure 2, showing separation assembly **14**, separate from a first leucocyte depletion assembly **13**.

While the October 17, 2003 Advisory Action states "[i]t would be obvious to one of ordinary skill in the art that if one wants to separate the blood into individual components, one would require separate filters for each component," this does not address the issue.

One reading Pall '070, that discloses fibrous leukocyte depletion media and membranes in separate devices, would not be led to combine both media into a single device (in effect, combining both devices into a single device), and would not be led to process a biological fluid by passing it through such a device. In accordance with Pall '070, the leukocyte depletion assembly (which includes a leukocyte depletion medium) is disclosed as being a distinct device from the non-centrifugal separation device (which includes a membrane) because, as is known in the art, the devices are operated differently.

When operating the non-centrifugal separation device disclosed in Pall '070, the biological fluid is directed tangentially or parallel to the separation medium's upstream surface. Plasma passes through the medium and through one outlet, and red blood cells and platelets (in the plasma-depleted fluid) pass tangentially or parallel to the medium's upstream surface and pass through another outlet without passing through the medium (i.e., the components do not pass from the upstream surface to the downstream surface). *See*, Figure 5 in Pall '070, showing plasma passing along fluid flow path **215** through the medium **216** from the upstream surface **216a** to the downstream surface **216b** and through the outlet **213**, and plasma-depleted fluid passing along fluid flow path **214** tangentially to surface **216a** and through the outlet **212** without passing through the medium **216**.

As Pall '070 explains, the biological fluid flows tangential or parallel to the separation medium and clogging by other components is minimized or prevented (*see*, for example, col. 18, lines 40-42; col. 20, lines 38-40, *see also*, Figure 5 as noted above, illustrating the

tangential flow and first and second outlets **212** and **213**). Thus, red blood cells and/or platelets pass parallel or tangential to the upstream surface without passing through the downstream surface of the membrane.

This is further reinforced by the portion of Pall '070 specifically relied on as supporting the June 10, 2003 Office Action's conclusion (*see*, page 7 of the Office Action, referring twice to col. 10, lines 21-39 of Pall '070). As stated at col. 10, lines 21-39 of Pall '070: "Tangential flow of a biological fluid parallel to the upstream surface of the separation medium permits the passage of plasma through the medium, while reducing the tendency of cellular components or platelets to adhere to the surface of the medium, thus assisting in the prevention of passage of platelets through the separation medium. The hydrodynamics of flow parallel to the surface are indeed believed to be such that during flow parallel to the surface, platelets develop a spin which causes them to be recovered from the surface."

In contrast, the leukocyte depletion assembly disclosed in Pall '070 (which is a distinct device from the non-centrifugal separation device) is operated differently. All of the biological fluid passes through the fibrous leukocyte depletion medium of a leukocyte depletion assembly wherein all of the fluid passes through the upstream surface and through the downstream surface of the medium (commonly referred to as "perpendicular" flow). Fluid does not flow tangentially or parallel to the upstream surface, rather, all of it passes through the downstream surface (*see*, for example, Figure 2, wherein the filtered fluid passes through the single outlet of first leukocyte depletion assembly **13**).

The Office Action has converted the tangential flow non-centrifugal separation device of Pall '070 into a perpendicular flow device. Such a force fitting is incorrect, particularly since Pall '070 explains why the tangential flow non-centrifugal separation device must be designed and operated the way it is. The Office Action eviscerates the teaching of the reference.

The Office Action also ignores other differences between non-centrifugal separation devices and leukocyte depletion assemblies including fibrous leukocyte depletion media. As is known in the art, a fibrous leukocyte depletion medium depletes leukocytes from the fluid by adsorption (wherein leukocytes stick to the fibers) and by sieving (wherein leukocytes are captured in, or excluded by, the pores of the medium). In other words, leukocytes accumulate in and on the fibrous leukocyte depletion medium. In contrast, the separation

medium in a non-centrifugal separation device minimizes the accumulation of material. For example, Pall '070 emphasizes "reducing the tendency of cellular components or platelets to adhere to the surface of the medium, thus assisting in the prevention of passage of platelets through the separation medium" (col. 10, lines 33-37). *See also,* col. 10, lines 40-42, "[c]logging of the separation medium by these other components [platelets and/or red cells] is minimized or prevented."

Since red blood cells and platelets pass parallel or tangential to the upstream surface of the membrane in a non-centrifugal separation device without passing through the downstream surface of the membrane, and since accumulation of the red blood cells and platelets on the membrane is minimized in such a device, one of ordinary skill in the art would not be led to include a fibrous leukocyte depletion medium in the separation device containing the membrane, as such a fibrous leukocyte depletion medium would interfere with the flow tangential or parallel to the upstream surface of the membrane, thus leading to clogging. The problem would be exacerbated by the accumulation of leukocytes in and on the fibrous leukocyte depletion medium, as this accumulation would block fluid flow through the medium.

The October 17, 2003 Advisory Action states "if clogging was a problem, applicant's arguments re clogging would also be true for the filters 12 and 13 in Fig. 2." This is simply incorrect. Clogging is a problem with respect to non-centrifugal separation devices because of the interference with tangential flow across the surface of the medium, and because of the accumulation of material in and on the medium. Filters 12 and 13 in Figure 2 are perpendicular flow filters that do not utilize tangential flow and are designed to allow the accumulation of material therein.

The portion of Pall '070 cited by the June 10, 2003 Office Action as supporting the statements about hold up volume (col. 28, lines 45-52; the Advisory Action refers to the "implied" concern about hold-up volume) discloses the use of gas to facilitate the recovery of biological fluid trapped during processing (*see*, col. 28, lines 56-58), and does not lead one to combine a fibrous leukocyte depletion medium and a membrane in a single device or to combine a fibrous red cell barrier medium and a membrane in a single device. While the Office Action refers to reducing volume hold-up as the rationale for modifying Pall '070, one of ordinary skill in the art would not be led to the modification stated in the Office Action to

reduce the hold up volume. Including a fibrous leukocyte depletion medium in the separation device with the membrane would, in view of the increase in clogging as explained above, adversely impact the operation of the device, if not rendering it inoperative. Furthermore, it would not reduce the hold up volume.

According to the Advisory Action, the present rejection takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made. However, for the reasons set forth above, the Office Action has reached conclusions not suggested by the cited reference. Rather than providing a suggestion in the prior art, the Office Action has improperly used Appellants' disclosure as a template to select elements from the cited reference and then used these elements as the basis for a rejection. The Federal Circuit has specifically rejected this analysis as impermissible hindsight. See, for example, In re Gorman, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

Accordingly, appellants submit that the rejection of the Group I claims is improper, and should be reversed.

The Group II Claims

The Group II claims, claims 2, 11, 19, 20 and 25, were rejected under 35 U.S.C. § 103 as unpatentable over Pall '070.

The rejection of the Group II claims is essentially the same as the rejection of the Group I claims, and suffers from the same deficiencies as set forth by Appellants above. For example, one reading Pall '070, that discloses fibrous red cell barrier/leukocyte depletion media and membranes in separate devices, would not be led to combine the media into a single device (in effect, combining both devices into a single device), and would not be led to process a biological fluid by passing it through such a device. In accordance with Pall '070, the two types of devices are operated differently, as is known in the art. Accordingly, Appellants submit the rejection of the Group II claims is improper for the same reasons the rejection of the Group I claims is improper, and the arguments above regarding the Group I claims are incorporated by reference herein.

The rejection of the Group II claims suffers from additional deficiencies.

In accordance with the Group II claims, the first filter element comprises a porous fibrous red cell barrier and a leukocyte depletion medium having a CWST of at least about 70

dynes/cm. Biological fluid passes through the filter element (and the filter) in a perpendicular flow manner. Since the element includes a red cell barrier medium, the flow of biological fluid passing through the filter significantly slows or stops when the red blood cells block the medium, thus minimizing the chance that a significant level of red blood cells reach a container downstream of the filter (*see,* present application, page 9, line 25 through page 10, line 25).

Non-centrifugal separation devices are operated to minimize accumulation on the membrane surface as such accumulation would lead to clogging (*See*, Pall '070, col. 10, lines 33-37 and lines 40-42). Thus, one of ordinary skill in the art would not be led to include a fibrous red cell barrier and leukocyte depletion medium in a non-centrifugal separation device containing the membrane, as the red cell barrier medium would, by its operation, significantly stop or slow flow through the barrier medium. Put another way, the use of a red cell barrier medium is antithetical to the non-centrifugal separation device.

Accordingly, for all the reason set forth above, appellants submit that the rejection of the Group II claims is improper, and should be reversed.

Conclusion

The subject matter of the appealed claims is neither taught nor suggested by the cited references and is clearly unobvious over the prior art. Accordingly, Appellants respectfully submit that the rejections of the pending claims are improper and should be reversed.

Respectfully submitted,
LEYDIG, VOIT & MAYER

Jeremy M. Jay
Registration No. 33,587

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Washington, D. C. 20005
Telephone: (202) 737-6770
Facsimile: (202) 737-6776
Date: 5 Jan. 2004

APPENDIX

1. A filter device for processing a biological fluid comprising:

a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet;

a filter disposed in the housing across the fluid flow path, the filter comprising:

a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and

a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element;

wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes and red blood cells therethrough.

2. A filter device for processing a biological fluid comprising:

a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet;

a filter disposed in the housing across the fluid flow path, the filter comprising:

a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and

a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element;

wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

4. The device of claim 1, wherein the first filter element comprises melt-blown fibers.

5. The device of claim 1, wherein the first filter element comprises at least two layers.

6. The device of claim 1, wherein the first filter element has a CWST of at least about 90 dynes/cm.

7. The device of claim 1, wherein the filter includes no more than one membrane.

9. A system for processing a biological fluid comprising:

the device of claim 1; and

at least a first container and a second container, the first and second containers being suitable for use with biological fluid, wherein the device is interposed between the first and second containers.

10. A method for processing a biological fluid comprising:

passing a red blood cell- and leukocyte-containing plasma-rich biological fluid into a filter device comprising a filter including a fibrous leukocyte depletion medium and a membrane; and

collecting, from the filter device, a filtered plasma-rich biological fluid substantially free of leukocytes and red blood cells.

11. A method for processing a biological fluid comprising:

passing a leukocyte-containing plasma-rich biological fluid [through] into a filter device comprising a filter including a fibrous red blood cell barrier medium and a membrane; and

collecting, from the filter device, a filtered plasma-rich biological fluid substantially free of leukocytes.

12. A method for processing a biological fluid comprising:

processing a biological fluid to provide a supernatant layer comprising a leukocyte-containing plasma-rich fluid, and a sediment layer comprising a red blood cell-containing fluid;

passing the leukocyte-containing plasma-rich fluid into a filter device comprising a filter including a fibrous leukocyte depletion medium and a membrane; and

collecting, from the filter device, a filtered plasma-rich fluid substantially free of red blood cells and leukocytes.

13. The method of claim 12 wherein the leukocyte-containing plasma-rich fluid comprises a leukocyte-and platelet-depleted biological fluid.

14. A method for processing a biological fluid comprising:

depleting leukocytes and platelets from a red blood cell-containing biological fluid to provide a leukocyte- and platelet-depleted red blood cell-containing biological fluid;

processing the leukocyte- and platelet-depleted red blood cell-containing biological fluid to provide a supernatant layer comprising plasma and a sediment layer comprising red blood cells;

passing the supernatant layer through a filter device comprising a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet; and a filter disposed in the housing across the fluid flow path, the filter comprising a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element; wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes and red blood cells therethrough; wherein the filter further depletes leukocytes from the supernatant layer and substantially prevents the passage of red blood cells therethrough; and

collecting plasma-rich fluid in a container downstream of the filter device, wherein the plasma-rich fluid is substantially free of red blood cells and leukocytes.

17. The device of claim 1, wherein the second filter element comprises a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers.

18. The device of claim 7, wherein the second filter element comprises a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers.

19. The device of claim 2, wherein the second filter element comprises a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers.

20. A filter device for processing a biological fluid comprising:

a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet;

a filter disposed in the housing across the fluid flow path, the filter comprising;

a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and

a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element;

wherein the filter includes no more than one membrane, and is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

21. A method for processing a biological fluid comprising:

passing a plasma-rich biological fluid through a filter device comprising a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet, and a filter disposed in the housing across the fluid flow path, the filter comprising a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers, the second filter element being disposed downstream of the first filter element;

wherein passing the plasma-rich biological fluid through the filter device depletes the biological fluid of leukocytes and red blood cells.

22. The method of claim 21, wherein passing the plasma-rich biological fluid through the filter device also depletes the biological fluid of platelets.

23. The method of claim 21, comprising passing about 500 ml to about 1000 ml of plasma-rich biological fluid through the filter device.

24. The filter device of claim 1, wherein the filter is arranged to substantially prevent the passage of platelets therethrough.

25. The filter device of claim 2, wherein the filter is arranged to substantially prevent the passage of platelets therethrough.

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The real party in interest is the Assignee, Pall Corporation.

Related appeals and interferences

None.

Status of Claims

As filed (with a preliminary amendment upon entering the National phase under 35 USC 371), the application contained claims 1-14 and 17-20. During prosecution, claims 3 and 8 were additionally cancelled, and claims 21-25 were added, so that claims 1, 2, 4-7, 9-14 and 17-25 are pending in the application. Claims 1, 2, 4-7, 9-14 and 17-25 are finally rejected. The rejection of claims 1, 2, 4-7, 9-14 and 17-25 is appealed and those claims appear in the Appendix.

Status of Amendments

There were no amendments filed pursuant to 37 C.F.R. §1.116.

Summary of Invention

The present invention pertains to filter devices and methods for providing a plasma-containing biological fluid (e.g., for use as a transfusion product) that has been depleted of leukocytes and red blood cells.

In one embodiment, the filter device for processing a biological fluid comprises a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet; a filter disposed in the housing across the fluid flow path, the filter comprising: a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element; wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes and red blood cells therethrough.

In another embodiment, the filter device for processing a biological fluid comprises a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet; a filter disposed in the housing across the fluid flow path, the filter comprising: a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element; wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

The benefits of such filters and using such filters are several-fold. The presence of leukocytes in transfusion products is undesirable, as they can cause adverse effects (e.g., a febrile reaction) in the patient receiving the transfusion. Moreover, the presence of a significant level of red blood cells in the transfusion product can lead to an adverse immune response by the patient.

Issues

The issues on appeal are:

Whether the invention defined by appealed claims 1, 2, 4-7, 9-14 and 17-25 would have been obvious under 35 U.S.C. § 103 to one of ordinary skill in the art in view of U.S. Patent No. 5,587,070 to Pall *et al.* (hereinafter referred to as "Pall '070").

Grouping of Claims

For the purposes of this appeal, there are two groups of claims to be given separate consideration. These claims do not stand or fall together.

The first group of claims (Group I) consists of independent claims 1, 10, 12, 14, and 21, and dependent claims 4-7, 9, 13, 17, 18, and 22-24. The second group of claims (Group II) consists of independent claims 2, 11, and 20, and dependent claims 19 and 25.

Argument

The Group I Claims

The Group I claims, claims 1, 4-7, 9, 10, 12-14, 17, 18, and 21-24, were rejected under 35 U.S.C. § 103 as unpatentable over Pall '070.

While the June 10, 2003 Office Action acknowledges that Pall '070 does not disclose the invention as claimed in the Group I claims, the Office Action states that Pall '070 teaches a filter comprising a porous fibrous leukocyte depletion medium having a CWST of greater than 70 dynes/cm, and teaches a filter of 5 microns or less, and concludes it would have been obvious to one of ordinary skill in the art at the time of the invention to put a fibrous leukocyte depletion filter and a membrane in the same housing in series to obtain the desired separation of biological fluids while reducing the volume hold-up of the biological fluids. The Office Action also refers to compactness, ease of fabrication, and less conduit length.

The Office Action's position is incorrect.

While Pall '070 refers to a porous fibrous leukocyte depletion medium and a membrane (the Office Action has noted references to a membrane as a separation medium in

the non-centrifugal separation device), there is no suggestion of placing them in the same housing (*cf.*, Figure 1 in the instant application).

Rather, '070 Pall discloses the media in separate devices, e.g., at col. 18, lines 43-50: "In the embodiment of the invention which includes a separation assembly **14**, preferably a non-centrifugal separation device, the supernatant layer (e.g., PRP) may be passed through a leucocyte depletion assembly, and then passed through the non-centrifugal separation device **14**, where it may be processed and separated into components. . ." *See also*, Figure 2, showing separation assembly **14**, separate from a first leucocyte depletion assembly **13**.

While the October 17, 2003 Advisory Action states "[i]t would be obvious to one of ordinary skill in the art that if one wants to separate the blood into individual components, one would require separate filters for each component," this does not address the issue.

One reading Pall '070, that discloses fibrous leukocyte depletion media and membranes in separate devices, would not be led to combine both media into a single device (in effect, combining both devices into a single device), and would not be led to process a biological fluid by passing it through such a device. In accordance with Pall '070, the leukocyte depletion assembly (which includes a leukocyte depletion medium) is disclosed as being a distinct device from the non-centrifugal separation device (which includes a membrane) because, as is known in the art, the devices are operated differently.

When operating the non-centrifugal separation device disclosed in Pall '070, the biological fluid is directed tangentially or parallel to the separation medium's upstream surface. Plasma passes through the medium and through one outlet, and red blood cells and platelets (in the plasma-depleted fluid) pass tangentially or parallel to the medium's upstream surface and pass through another outlet without passing through the medium (i.e., the components do not pass from the upstream surface to the downstream surface). *See*, Figure 5 in Pall '070, showing plasma passing along fluid flow path **215** through the medium **216** from the upstream surface **216a** to the downstream surface **216b** and through the outlet **213**, and plasma-depleted fluid passing along fluid flow path **214** tangentially to surface **216a** and through the outlet **212** without passing through the medium **216**.

As Pall '070 explains, the biological fluid flows tangential or parallel to the separation medium and clogging by other components is minimized or prevented (*see*, for example, col. 18, lines 40-42; col. 20, lines 38-40, *see also*, Figure 5 as noted above, illustrating the

tangential flow and first and second outlets **212** and **213**). Thus, red blood cells and/or platelets pass parallel or tangential to the upstream surface without passing through the downstream surface of the membrane.

This is further reinforced by the portion of Pall '070 specifically relied on as supporting the June 10, 2003 Office Action's conclusion (*see*, page 7 of the Office Action, referring twice to col. 10, lines 21-39 of Pall '070). As stated at col. 10, lines 21-39 of Pall '070: "Tangential flow of a biological fluid parallel to the upstream surface of the separation medium permits the passage of plasma through the medium, while reducing the tendency of cellular components or platelets to adhere to the surface of the medium, thus assisting in the prevention of passage of platelets through the separation medium. The hydrodynamics of flow parallel to the surface are indeed believed to be such that during flow parallel to the surface, platelets develop a spin which causes them to be recovered from the surface."

In contrast, the leukocyte depletion assembly disclosed in Pall '070 (which is a distinct device from the non-centrifugal separation device) is operated differently. All of the biological fluid passes through the fibrous leukocyte depletion medium of a leukocyte depletion assembly wherein all of the fluid passes through the upstream surface and through the downstream surface of the medium (commonly referred to as "perpendicular" flow). Fluid does not flow tangentially or parallel to the upstream surface, rather, all of it passes through the downstream surface (*see*, for example, Figure 2, wherein the filtered fluid passes through the single outlet of first leukocyte depletion assembly **13**).

The Office Action has converted the tangential flow non-centrifugal separation device of Pall '070 into a perpendicular flow device. Such a force fitting is incorrect, particularly since Pall '070 explains why the tangential flow non-centrifugal separation device must be designed and operated the way it is. The Office Action eviscerates the teaching of the reference.

The Office Action also ignores other differences between non-centrifugal separation devices and leukocyte depletion assemblies including fibrous leukocyte depletion media. As is known in the art, a fibrous leukocyte depletion medium depletes leukocytes from the fluid by adsorption (wherein leukocytes stick to the fibers) and by sieving (wherein leukocytes are captured in, or excluded by, the pores of the medium). In other words, leukocytes accumulate in and on the fibrous leukocyte depletion medium. In contrast, the separation

medium in a non-centrifugal separation device minimizes the accumulation of material. For example, Pall '070 emphasizes "reducing the tendency of cellular components or platelets to adhere to the surface of the medium, thus assisting in the prevention of passage of platelets through the separation medium" (col. 10, lines 33-37). *See also,* col. 10, lines 40-42, "[c]logging of the separation medium by these other components [platelets and/or red cells] is minimized or prevented."

Since red blood cells and platelets pass parallel or tangential to the upstream surface of the membrane in a non-centrifugal separation device without passing through the downstream surface of the membrane, and since accumulation of the red blood cells and platelets on the membrane is minimized in such a device, one of ordinary skill in the art would not be led to include a fibrous leukocyte depletion medium in the separation device containing the membrane, as such a fibrous leukocyte depletion medium would interfere with the flow tangential or parallel to the upstream surface of the membrane, thus leading to clogging. The problem would be exacerbated by the accumulation of leukocytes in and on the fibrous leukocyte depletion medium, as this accumulation would block fluid flow through the medium.

The October 17, 2003 Advisory Action states "if clogging was a problem, applicant's arguments re clogging would also be true for the filters 12 and 13 in Fig. 2." This is simply incorrect. Clogging is a problem with respect to non-centrifugal separation devices because of the interference with tangential flow across the surface of the medium, and because of the accumulation of material in and on the medium. Filters 12 and 13 in Figure 2 are perpendicular flow filters that do not utilize tangential flow and are designed to allow the accumulation of material therein.

The portion of Pall '070 cited by the June 10, 2003 Office Action as supporting the statements about hold up volume (col. 28, lines 45-52; the Advisory Action refers to the "implied" concern about hold-up volume) discloses the use of gas to facilitate the recovery of biological fluid trapped during processing (*see*, col. 28, lines 56-58), and does not lead one to combine a fibrous leukocyte depletion medium and a membrane in a single device or to combine a fibrous red cell barrier medium and a membrane in a single device. While the Office Action refers to reducing volume hold-up as the rationale for modifying Pall '070, one of ordinary skill in the art would not be led to the modification stated in the Office Action to

reduce the hold up volume. Including a fibrous leukocyte depletion medium in the separation device with the membrane would, in view of the increase in clogging as explained above, adversely impact the operation of the device, if not rendering it inoperative. Furthermore, it would not reduce the hold up volume.

According to the Advisory Action, the present rejection takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made. However, for the reasons set forth above, the Office Action has reached conclusions not suggested by the cited reference. Rather than providing a suggestion in the prior art, the Office Action has improperly used Appellants' disclosure as a template to select elements from the cited reference and then used these elements as the basis for a rejection. The Federal Circuit has specifically rejected this analysis as impermissible hindsight. See, for example, In re Gorman, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

Accordingly, appellants submit that the rejection of the Group I claims is improper, and should be reversed.

The Group II Claims

The Group II claims, claims 2, 11, 19, 20 and 25, were rejected under 35 U.S.C. § 103 as unpatentable over Pall '070.

The rejection of the Group II claims is essentially the same as the rejection of the Group I claims, and suffers from the same deficiencies as set forth by Appellants above. For example, one reading Pall '070, that discloses fibrous red cell barrier/leukocyte depletion media and membranes in separate devices, would not be led to combine the media into a single device (in effect, combining both devices into a single device), and would not be led to process a biological fluid by passing it through such a device. In accordance with Pall '070, the two types of devices are operated differently, as is known in the art. Accordingly, Appellants submit the rejection of the Group II claims is improper for the same reasons the rejection of the Group I claims is improper, and the arguments above regarding the Group I claims are incorporated by reference herein.

The rejection of the Group II claims suffers from additional deficiencies.

In accordance with the Group II claims, the first filter element comprises a porous fibrous red cell barrier and a leukocyte depletion medium having a CWST of at least about 70

dynes/cm. Biological fluid passes through the filter element (and the filter) in a perpendicular flow manner. Since the element includes a red cell barrier medium, the flow of biological fluid passing through the filter significantly slows or stops when the red blood cells block the medium, thus minimizing the chance that a significant level of red blood cells reach a container downstream of the filter (*see,* present application, page 9, line 25 through page 10, line 25).

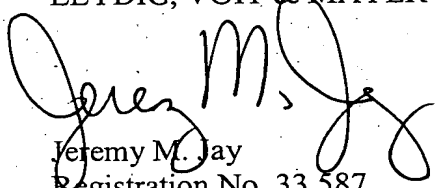
Non-centrifugal separation devices are operated to minimize accumulation on the membrane surface as such accumulation would lead to clogging (*See*, Pall '070, col. 10, lines 33-37 and lines 40-42). Thus, one of ordinary skill in the art would not be led to include a fibrous red cell barrier and leukocyte depletion medium in a non-centrifugal separation device containing the membrane, as the red cell barrier medium would, by its operation, significantly stop or slow flow through the barrier medium. Put another way, the use of a red cell barrier medium is antithetical to the non-centrifugal separation device.

Accordingly, for all the reason set forth above, appellants submit that the rejection of the Group II claims is improper, and should be reversed.

Conclusion

The subject matter of the appealed claims is neither taught nor suggested by the cited references and is clearly unobvious over the prior art. Accordingly, Appellants respectfully submit that the rejections of the pending claims are improper and should be reversed.

Respectfully submitted,
LEYDIG, VOIT & MAYER



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APPENDIX

1. A filter device for processing a biological fluid comprising:

a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet;

a filter disposed in the housing across the fluid flow path, the filter comprising:

a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and

a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element;

wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes and red blood cells therethrough.

2. A filter device for processing a biological fluid comprising:

a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet;

a filter disposed in the housing across the fluid flow path, the filter comprising:

a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and

a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element;

wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

4. The device of claim 1, wherein the first filter element comprises melt-blown fibers.

5. The device of claim 1, wherein the first filter element comprises at least two layers.

6. The device of claim 1, wherein the first filter element has a CWST of at least about 90 dynes/cm.

7. The device of claim 1, wherein the filter includes no more than one membrane.

9. A system for processing a biological fluid comprising:

the device of claim 1; and

at least a first container and a second container, the first and second containers being suitable for use with biological fluid, wherein the device is interposed between the first and second containers.

10. A method for processing a biological fluid comprising:

passing a red blood cell- and leukocyte-containing plasma-rich biological fluid into a filter device comprising a filter including a fibrous leukocyte depletion medium and a membrane; and

collecting, from the filter device, a filtered plasma-rich biological fluid substantially free of leukocytes and red blood cells.

11. A method for processing a biological fluid comprising:

passing a leukocyte-containing plasma-rich biological fluid [through] into a filter device comprising a filter including a fibrous red blood cell barrier medium and a membrane; and

collecting, from the filter device, a filtered plasma-rich biological fluid substantially free of leukocytes.

12. A method for processing a biological fluid comprising:

processing a biological fluid to provide a supernatant layer comprising a leukocyte-containing plasma-rich fluid, and a sediment layer comprising a red blood cell-containing fluid;

passing the leukocyte-containing plasma-rich fluid into a filter device comprising a filter including a fibrous leukocyte depletion medium and a membrane; and

collecting, from the filter device, a filtered plasma-rich fluid substantially free of red blood cells and leukocytes.

13. The method of claim 12 wherein the leukocyte-containing plasma-rich fluid comprises a leukocyte-and platelet-depleted biological fluid.

14. A method for processing a biological fluid comprising:

depleting leukocytes and platelets from a red blood cell-containing biological fluid to provide a leukocyte- and platelet-depleted red blood cell-containing biological fluid;

processing the leukocyte- and platelet-depleted red blood cell-containing biological fluid to provide a supernatant layer comprising plasma and a sediment layer comprising red blood cells;

passing the supernatant layer through a filter device comprising a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet; and a filter disposed in the housing across the fluid flow path, the filter comprising a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element; wherein the filter is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes and red blood cells therethrough; wherein the filter further depletes leukocytes from the supernatant layer and substantially prevents the passage of red blood cells therethrough; and

collecting plasma-rich fluid in a container downstream of the filter device, wherein the plasma-rich fluid is substantially free of red blood cells and leukocytes.

17. The device of claim 1, wherein the second filter element comprises a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers.

18. The device of claim 7, wherein the second filter element comprises a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers.

19. The device of claim 2, wherein the second filter element comprises a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers.

20. A filter device for processing a biological fluid comprising:

a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet;

a filter disposed in the housing across the fluid flow path, the filter comprising;

a first filter element comprising a porous fibrous red cell barrier and leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and

a second filter element comprising a porous membrane having a pore size of about 5 micrometers or less, said second filter element being disposed downstream of the first filter element;

wherein the filter includes no more than one membrane, and is arranged to allow plasma to pass therethrough and substantially prevent the passage of leukocytes therethrough.

21. A method for processing a biological fluid comprising:

passing a plasma-rich biological fluid through a filter device comprising a housing having an inlet and an outlet and defining a fluid flow path between the inlet and the outlet, and a filter disposed in the housing across the fluid flow path, the filter comprising a first filter element comprising a porous fibrous leukocyte depletion medium having a CWST of at least about 70 dynes/cm; and a second filter element comprising a porous membrane having a pore size in the range of from about 0.3 to about 3 micrometers, the second filter element being disposed downstream of the first filter element;

wherein passing the plasma-rich biological fluid through the filter device depletes the biological fluid of leukocytes and red blood cells.

22. The method of claim 21, wherein passing the plasma-rich biological fluid through the filter device also depletes the biological fluid of platelets.

23. The method of claim 21, comprising passing about 500 ml to about 1000 ml of plasma-rich biological fluid through the filter device.

24. The filter device of claim 1, wherein the filter is arranged to substantially prevent the passage of platelets therethrough.

25. The filter device of claim 2, wherein the filter is arranged to substantially prevent the passage of platelets therethrough.